Prostate Cancer Management and Referral Guidance

The Prostate Cancer Management and Referral Guidance has been developed to help primary care health professionals manage men with symptoms suggestive of prostate cancer or men who request testing for prostate cancer.

The guidance provides an evidenced-based, best practice pathway of care. It includes two flow charts – one for men with symptoms and one for men without symptoms – as well as a set of explanatory notes.

The guidance has been developed by the primary care sub-group of the Prostate Cancer Working Group. The Working Group is overseeing the implementation of the Ministry of Health's *Prostate Cancer Awareness and Quality Improvement Programme*.[1]

The programme aims to raise awareness of prostate cancer, improve the quality of prostate cancer care, and improve outcomes through improved survival and reduced morbidity from advanced disease while also reducing the harms caused by over treatment.

There is currently no good quality evidence that routine prostate specific antigen (PSA) testing of men can effectively reduce deaths caused by prostate cancer.[2] As such, population-based screening for prostate cancer is not recommended in New Zealand.[3]

There is mixed information and understanding among health professionals and the public about testing for prostate cancer and the use of the PSA blood test. While routine screening for prostate cancer is not considered appropriate given current evidence, many men ask to be tested. Choosing whether or not to be tested for prostate cancer is every man's right.

Doctors and other health professionals have a duty, under the Code of Health and Disability Services Consumers' Rights Regulations 1996, to respond to men requesting testing by providing good, balanced information on prostate cancer and the possible benefits and harms of testing and treatment. Therefore primary care has a central role in helping men make informed decisions about prostate cancer testing and in managing men who have been diagnosed with prostate cancer.

This guidance has been provided to all public health organisations and district health boards for implementation into local practice and systems such as care pathways.

This guidance will be reviewed on an annual basis and revised versions published.

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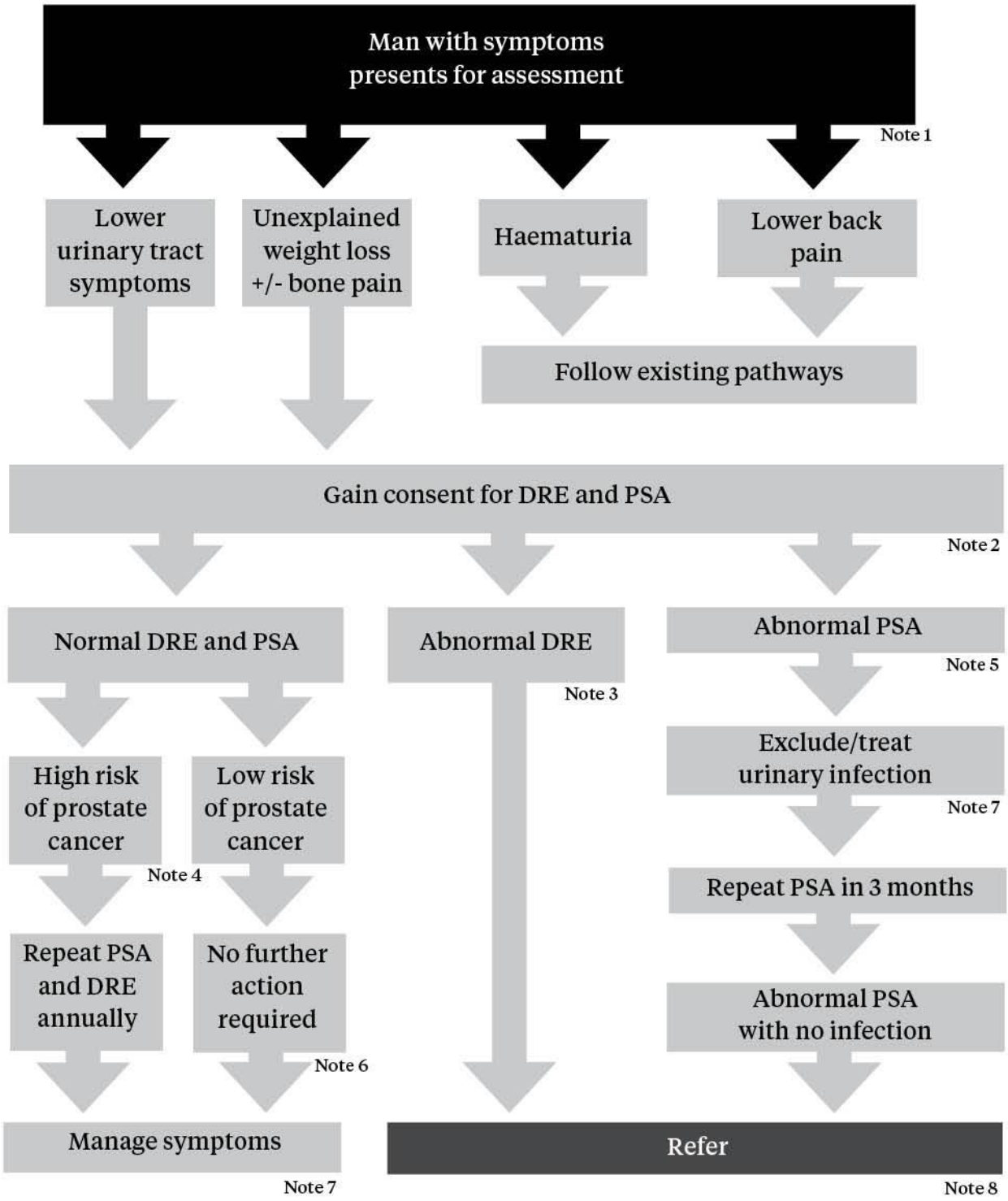
Men with symptoms



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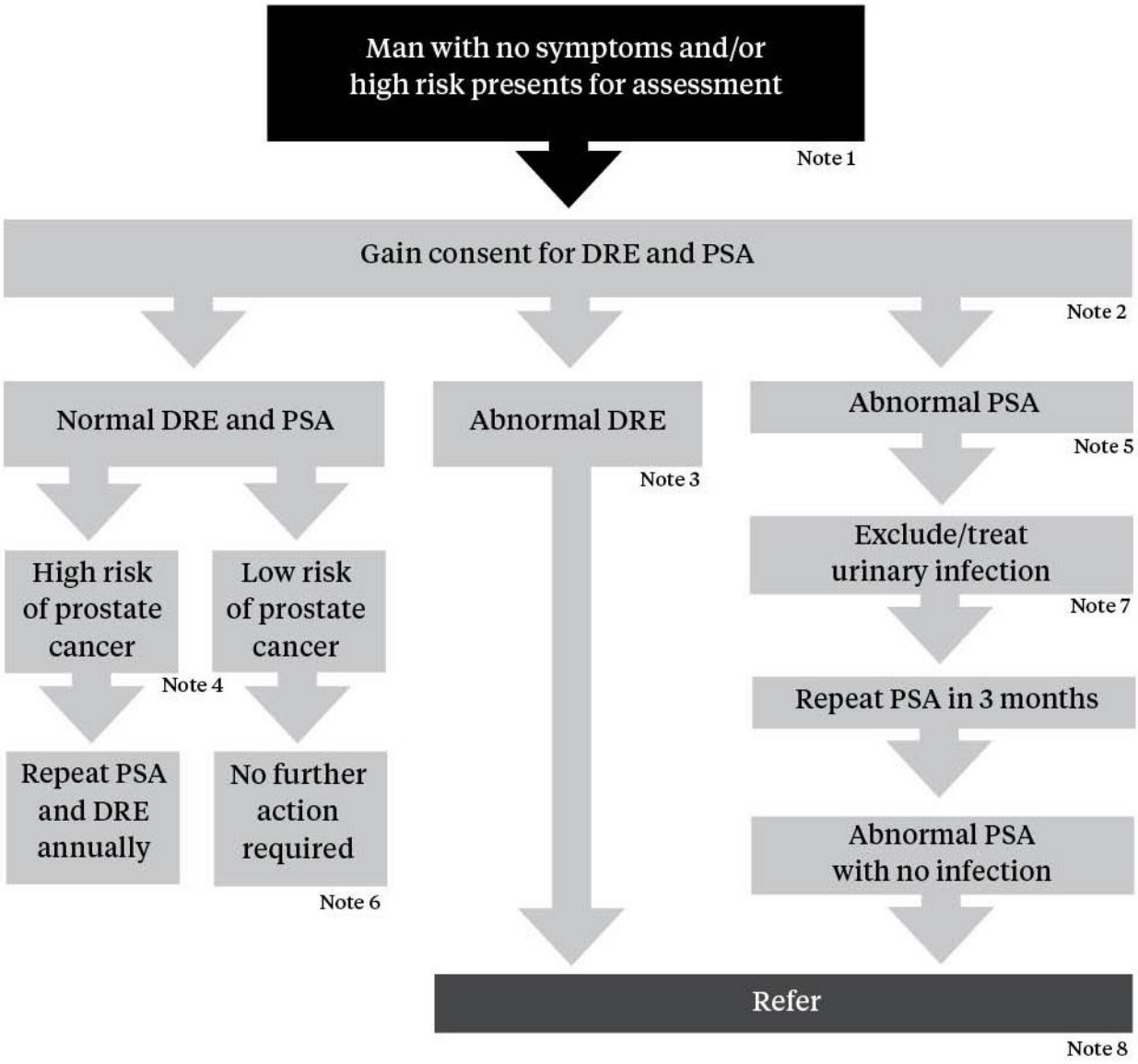
Men with no symptoms



Note 1: Preliminary considerations

1.1 Age

Prostate cancer is rare in men under 40 years. The risk of having prostate cancer increases in men over the age of 50. Although the evidence of benefit from RCTs is conflicting, it is men between the ages of 50 and 70 who are most likely to benefit from prostate cancer testing.[4,5]

There is no strong evidence that screening men aged over 70 reduces mortality from prostate cancer. It is recommended that men aged over 70 who have a normal prostate on digital rectal examination (DRE) and have had previously normal prostate specific antigen (PSA) tests should be advised that they do not require further PSA testing.

Men over the age of 70 with a family history of prostate cancer and those with a previously raised PSA may be considered suitable for further monitoring if they are otherwise well and have a life expectancy greater than 10 years.[6]

1.2 Family history

If a man has one first-order relative (father or brother) with prostate cancer then his risk of developing prostate cancer is at least doubled. If two or more first-order relatives are affected, the risk increases by 5–11 times.[7]

A small subpopulation of men with prostate cancer (about 9%) have the true hereditary form of the disease. This is defined as three or more affected relatives, or at least two relatives who have developed early onset disease (before the age of 55 years). Patients with hereditary prostate cancer usually have an onset six to seven years earlier than spontaneous cases, but do not differ in other ways. The risk is higher if more than one close relative is affected and is also higher if a close relative is diagnosed at a younger age (under 65 years).[8]

1.3 Ethnicity

Māori men are less likely to be diagnosed with prostate cancer than non-Māori men but are twice as likely to die from the disease.

The cancer registrations and mortality data for 2011 show that the prostate cancer registration rate was 81.4 per 100,000 for Māori compared with 99.0 per 100,000 for non-Māori, while the mortality rate was 22.1 per 100,000 for Māori compared with 16.2 per 100,000 for non-Māori. [9,10,11]

There are a number of reasons why a greater proportion of Māori men are dying from prostate cancer. These include presenting with advanced disease, being less aware of prostate cancer symptoms or being disadvantaged by inequitable access to appropriate care.

Whilst recognising a DRE may present a barrier to testing for some men, a more tailored approach may be required for Māori or Pacific men that also takes their cultural values into account.

1.4 Other demographic data affecting testing

The level of access to health care is associated with the quality of the outcome in men with prostate cancer. Living in rural or remote areas and deprived circumstances are factors that are likely to impact on health outcomes. There is variability in PSA testing across New Zealand with greater prevalence in men living in decile 1 compared with men from decile 10 communities.[11]

1.5 Lifestyle factors

There is variable evidence that the following factors increase the risk of men developing prostate cancer:[12 13 14 15]

- obesity
- smoking
- prostatitis
- sexually transmitted diseases
- diet.

Note 2: Informed consent

It is essential that doctors and other health professionals obtain informed consent before undertaking a DRE or PSA test.

Doctors and other health professionals have a duty, under the Code of Health and Disability Services Consumers' Rights Regulations 1996, to provide patients who request testing with good, balanced information on prostate cancer and the possible benefits and harms of testing and treatment.[16,17]

Best practice involves presenting the extent of these harms and benefits in a way that men and whānau can understand. This includes presenting absolute as opposed to relative numbers in terms of risk changes, harms and benefits. For example, "the benefit of prostate cancer screening is that out of 1000 men tested one death will be prevented" versus "there is a 40% reduction in the death rate from prostate cancer screening". [4]

Note 3: Digital rectal examination

3.1 Abnormal DRE

Most prostate cancers are located in the peripheral zone of the prostate and some may be detected by DRE.[18] Prostate cancer may present as a hard discrete nodule or with asymmetry of the gland. In about 18% of patients prostate cancer is detected by an abnormal DRE alone, irrespective of the PSA level. An abnormal DRE requires referral and is a strong indication for prostate biopsy as it is predictive of more aggressive prostate cancer.

3.2 When a DRE is a barrier to testing

Some prostate cancers do not produce PSA. PSA tests in isolation can still be helpful when a DRE is declined. But, in about 18% of all patients, prostate cancer is detected by a suspect DRE alone, irrespective of the PSA level.[19,20]

Note 4: High risk groups

4.1 Family history

Men at higher risk of developing prostate cancer are those with a strong family history of this disease. If a man has one first-order relative (father or brother) with prostate cancer then his risk of developing prostate cancer is at least doubled. If two or more first-order relatives are affected, the risk increases by 5–11 times.

4.2 Increase in PSA/rate of change

Men in the high risk group should have an annual PSA and DRE. If the PSA is below the normal referral criteria but the rate of change of PSA is >1.5 ng/mL per year, the man should be referred for assessment.

Note 5: PSA testing

5.1 PSA

PSA is produced almost exclusively by the epithelial cells of the prostate. For practical purposes it is organ-specific but not cancer-specific. Therefore, PSA levels may be elevated in the presence of benign prostatic hypertrophy (BPH), prostatitis and other non-malignant conditions.[21]

PSA should not be measured within three days of ejaculation as this can result in an elevated reading. A DRE can also result in an elevated PSA, so blood should be collected before this examination. Prostate biopsies can lead to either upward or downward movement in the PSA, which may persist for months after the procedure.

The higher the PSA level, the more likely it is that a cancer is present.[22] If the value is between 4.0

and 10.0 ng/mL there is an approximately 40% chance of cancer being detected on prostate biopsy. The incidence of cancer may actually be slightly higher than this, because low-volume cancers can be 'missed' even when systematic zonal biopsies are taken.[23] Other explanations for a small elevation in PSA are BPH and prostatitis.

A PSA >10.0 ng/mL indicates a 67% chance that a cancer is present. Values this high are rarely the result of BPH, but prostatitis can cause a significant and rapid rise in PSA.

A PSA >20.0 ng/mL means a cancer is highly likely to be present and metastases can sometimes already be demonstrated on bone or CT scan. Prostatitis is the most common alternative cause of this level of PSA elevation.

An elevated PSA may be transient. Therefore (in the absence of an abnormal DRE) the PSA should always be repeated after an interval of 6 to 12 weeks.

The level of PSA is a continuous parameter: the higher the value, the more likely it is that prostate cancer exists. Many men may have prostate cancer despite low levels of PSA.[24]

5.2 Age related PSA levels

The trigger for referral to a urologist is age dependent because the benefits of early diagnosis reduce with increasing age.[25,26] At 70 years of age a man diagnosed with prostate cancer as a result of an elevated PSA has an approximately 50% chance that the cancer will become symptomatic in his lifetime. By 75 years this risk has reduced to 33%.[27]

General practitioners should refer patients to an urologist according to the following criteria:

- men aged ≤70 years when the PSA is elevated to ≥4.0 ng/mL
- men aged 71–75 years when the PSA is elevated to ≥10.0 ng/mL
- men aged ≥76 years when the PSA is elevated to ≥20 ng/mL.

Note 6: Further testing for men with low risk and a normal DRE and PSA

Some men will seek further PSA testing regardless of any symptoms or risk to indicate this is clinically warranted. The role of primary care is to ensure men have clear and balanced information about the advantages, disadvantages and limitations of the PSA test and treatment for prostate cancer. This will help men make informed decisions about whether to have the test.

Evidence does not indicate regular PSA testing for low risk, asymptomatic men reduces prostate cancer mortality. Refer to step one of the *men with no symptoms* flow chart to guide the management of men without symptoms requesting a PSA test.

Note 7: Men with symptoms

7.1 Lower urinary tract symptoms

Lower urinary tract symptoms (LUTS) become more prevalent in men with increasing age. These symptoms include decreased force of the urine stream, passing urine more frequently, sometimes with delay in starting (hesitancy) and dribbling at the end of the urine flow. The most common cause of these symptoms is BPH and bladder dysfunction but a wide range of non-prostatic causes such as diabetes, spinal nerve problems and bladder abnormalities can present in a similar manner.

Men with LUTS symptoms have a small, increased risk of having prostate cancer compared with men without symptoms. The presence of these symptoms also increases the chance that prostate cancer will be found, be it incidental or potentially life threatening.[28,29] The small number of men whose LUTS are caused by prostate cancer are likely to have more advanced disease than if the cancer was detected while asymptomatic.[30] For this reason all men presenting with LUTS require an appropriate history and clinical examination.

7.2 Symptoms related to systemic effects of prostate cancer

Men may present with systemic features of malignancy related to prostate cancer. These may include lethargy, anaemia, weight loss (especially in the elderly), anorexia and lymphadenopathy. Bone pain, especially in the pelvis and lower spine, is sometimes seen in advanced disease.

Note 8: Urgency of referral

8.1 Immediate referral

Indications for immediate referral are:

- prostate cancer associated with spinal cord compression or high risk of spinal cord compression
- prostate cancer associated with renal failure.

Spinal cord compression

Spinal cord compression occurs in up to 12% of metastatic prostate cancer patients. Advanced disease should be considered in patients presenting with back pain, even in the absence of neurologic symptoms. Spinal cord compression is an oncological and surgical emergency. Delays in referral and diagnosis may influence functional outcome. Early diagnosis and rapid treatment of spinal cord compression is crucial for neurological recovery.[31]

Renal failure

Symptoms of renal failure include tiredness, lack of energy, nausea, peripheral oedema and poor appetite. Renal failure may be caused by ureteric obstruction from metastatic spread to retroperitoneal lymph nodes or from locally advanced prostate cancer causing ureteric obstruction at the level of the bladder base.[32] Prostate cancer that causes chronic urinary retention, through prostatic obstruction, can also cause hydronephrosis and renal failure.

Symptomatic patients with an abnormally high serum creatinine (eGFR<30) with either urinary retention or hydronephrosis (as shown on imaging) require immediate referral because of the possible requirement for urinary drainage. This may involve nephrostomy drainage, ureteric stenting or urinary catheterisation for men with urinary retention.[33]

8.2 Urgent referral

Indications for urgent referral (i.e. within 14 days) are:

- patients with a hard, irregular prostate typical of prostate cancer
- patients with a normal prostate, but rising/raised age-specific prostate specific antigen (PSA), with or without lower urinary tract symptoms.

Men presenting with a clinically malignant prostate are more likely to have advanced disease. In these cases PSA should be measured and the result should accompany the referral. If the PSA is normal then the patient must still be referred for assessment because a small percentage of highly anaplastic (therefore aggressive) prostate cancers present with a normal PSA.

An urgent referral is not needed if the prostate is simply enlarged and the PSA is normal.

8.3 Faster cancer treatment indicators and health target

All district health boards collect and report information on patients who have been referred urgently with a high-suspicion of cancer. The indicators set out the timeframes for patients (with a high-suspicion of cancer) to access services along the cancer diagnosis and treatment pathway.

The indicators are:

- 31 days from decision to treat to first treatment
- 62 days from referral receipt by the hospital to first treatment.

From 1 October 2014 the new health target for faster cancer treatment is 90 percent of patients to receive their first treatment within 62 days of seeing their GP, by June 2017.

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